

REMARKS

Applicant acknowledges that claims 1-12 have been withdrawn and only claim 13 remains.

Regarding the objection to the specification, claim 13 and drawings for not incorporating the sequence numbers in same, Applicant has made the preceding changes in the specification paragraphs, claim 13 and FIGs. 1, 2, and 3. In response to ¶5, Applicant has entered the priority paragraph in the preceding changes to the Specification.

In response to ¶ 6, claim 13 was rejected as indefinite for using “shown”, and it was recommended that “set forth” be used instead. Please refer to amended claim 13, which no longer includes “shown”.

In response to the ¶ 7 claim rejection over 35 USC §101, the Applicant has amended claim 13 and added “isolated” as thoughtfully recommended by the Examiner. Applicant respectfully requests that this ground for rejection now be withdrawn.

In ¶ 8, the Office Action rejected claim 13 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification as to enable one skilled in the art to make or use the invention. Suggesting a lack of enablement based on how to make the invention, the Office Action noted that the promoter sequence was provided, but there was no description of its isolation and verification. Suggesting a lack of enablement based on enablement of how to make the invention, the Office Action cited two references. The first was cited in support of the unexpectedness of expression patterns in different plant species (Oommen et al. 1994 Plant Cell 6:1789-1803). The second was Kagaya et al. (1995, Mol. Gen. Genet. 248:668-74), which was cited for disclosing a promoter with two elements, one negative and one positive, in developmentally regulating mesophyll cell-specific expression.

In response to the first ground, Applicant responds that isolation of promoters was well known in the art at the time of the filing of the patent application in 1999. Nevertheless, for specific enablement of Applicant’s invention of the DNA encoding a promoter, the Applicant published (prior to the earliest filing date) two articles: Deutsch CE and I. Winicov. 1995, Post-Translational Regulation of a Salt-Inducible Alfalfa Gene Encoding a Putative Chimeric Proline-Rich Cell Wall Protein. Plant Mol. Biol. 27:411-18 (Deutsch”); and Bastola DR, Pethe VV, and I Winicov. 1998. Plant Mol. Biol 38:1123-35 (“Bastola”). Deutsch discloses the DNA sequence

for the MsPRP2 protein, as well as flanking 5' and 3' sequences, the 5' sequence later discovered to contain a small part of the MsPRP2 promoter. The DNA sequence was obtained by inserting a genomic library of alfalfa into the Sal I site of Lambda FixII (Stratagene) and screening by hybridization to ³²P-labelled fragments prepared by random priming of the electrophoretically purified insert in clone *pA9*. One clone containing an 18 kb insert was digested with *Sal* I. A 4.5 kb Eco RI fragment of the insert that hybridized to the cDNA in clone *pA9*, was subcloned into the Eco RI site of pBlue script plasmid DNA (Stratagene), and the construct transformed into *E. coli* JM109 (Promega). Plasmid DNA containing the fragment was isolated and sequenced. The coding region was 1143 bp and the upstream fragment was 329 bp.

Blastola goes on to explain how the MsPRP2 promoter sequence was obtained. Blastola tells how the research team returned to the genomic clone in Lambda FixII that was shown to contain the insert of the MsPRP2 gene and mapped it. A 2900 bp fragment upstream of the coding sequence was subcloned into pUC19 and was shown to overlap the 5' end of the 4.5 kb EcoRI genomic fragment (sequenced by Deutsch). The double-stranded DNA sequence of the promoter region was determined using the Sequenase kit (US Biochemicals) according to the protocol provided by the supplier. This nucleotide sequence is shown in the instant patent application as SEQ ID NO 1 and has been submitted to GenBank as accession number AF028841. Note that the Deutsch reference is cited in the patent application at page 5, lines 26-28 and numerous other places.

In addition, the patent application discloses some of the methodology used to obtain the purified DNA (see pages 5-6). Purified Alfin1 protein was used in a random DNA binding assay to identify the MsPRP2 promoter. Then the bound DNA was purified by four rounds of PCR amplification and binding, followed by cloning of the isolated sequences. Then the bound sequences were determined and compared with other plants and were found in a wide variety of root-specific promoters (Table 2). Applicant believes that the specification and prior publications enable one skilled in the art to make the invention and that this portion of the rejection may be withdrawn.

For the second ground, Applicant notes that both Oommen and Kagaya discuss promoters for developmentally related genes. Oommen discusses the alfalfa IFR gene which is under not only developmental but also elicitor/infection control. Kagaya discloses that the Aldolase P (AldP) gene is under the control of two elements, a negative element and a positive element that

is not only developmentally regulated but also induced by light. It was well known in the art that developmentally related genes are intricately controlled because their production must be timed and limited to certain cell types and subtypes. It was well known, as confirmed by Oommen, that developmentally regulated promoters often do not transfer well from one plant system to another. On the other hand, Kagaya states in the last sentence of the abstract: "The results suggest that the AldP gene promoter of rice, a monocot promoter, can function in an essentially physiological manner in the Dicot tobacco plant." Thus, Kagaya supports the transferability of even a developmentally regulated promoter from a monocot to the dicot tobacco.

In contrast, the MsPRP2 promoter is not developmentally related but rather is constitutively produced. The specification describes the MsPRP2 "fragment [as] a constitutively expressed alfalfa gene (page 15, lines 15-16, citing to a Deutch and Winicov, 1994, reference). The specificity of the MsPRP2 promoter is discussed on page 16, lines 1-3: "This transcriptional activation was root specific, since leaves from the same transgenic plants showed increased Alfin1 mRNA levels without a concomitant increase in MsPRP2 transcripts..."

The Office Action stated that there was only a hypothetical example of how to use the invention. In the attached declaration by inventor Ilga Winicov, additional experimentation and successful expression of the endogenous gene GFP under the control of the MsPRP2 promoter is reported.

Because 1) the information of developmentally regulated promoters does not bring into question the transferability of the inventive constitutive promoter and 2) Kagaya indicates that a monocot developmentally regulated promoter "can function in an essentially physiological manner in the dicot", the references do not support questioning the enablement for the inventive constitutive promoter MsPRP2. Therefore, Applicant believes that this ground for nonenablement may be withdrawn.

Applicants have made an earnest attempt to place this case in condition for allowance. In light of the remarks set forth above, Applicants respectfully request reconsideration and allowance of claims 1 and 6-21. If there are matters which can be discussed by telephone to further the prosecution of this Application, Applicants invite the Examiner to call the undersigned attorney at the Examiner's convenience.

A petition for extension of time is attached to this paper, along with the respective extension fee due. The Commissioner is hereby authorized to charge any additional fees that may be due in connection with this filing to Deposit Account No. **17-0055**.

Respectfully submitted,
QUARLES & BRADY STREICH LANG, LLP

Dated: June 10, 2004

By: Barbara J. Luther
Barbara J. Luther, Reg. No. 33,954

Attorney Docket No. 112624.00018
Address all correspondence to:
Two North Central Avenue
Phoenix, AZ 85004
Telephone: (602) 230-5502
Facsimile: (602) 229-5690